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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,403	06/20/2005	Jose Manuel Francisco Lara Ochoa	2099.0090000/VLC/UWJ	3497

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STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1614	

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11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,403	OCHOA, JOSE MANUEL FRANCISCO LARA	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-39, and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/2/06, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 1, 3-9, and 11 are currently pending in this application and are the subject of this Office action.

Claims 2, and 10 are canceled.

Response to applicant's arguments/remarks

Rejection under 102(e)

Applicant contends that this rejection should be withdrawn because of the following reasons:

1) Patent '957 does not teach a solid formulation comprising metformin and glimepiride in the relative weight ratios of said ingredients recited in the instant claims.

2) The preferred combination of metformin to sulfonylurea in the '957 patent is in the range of 75:1 to 250:1;

3) Not all metformin/sulfonylurea combinations exhibit synergistic effect. Thus, the effect of using the presently claimed formulation in the claimed ratios is unexpected. The claimed ratio of metformin and glimepiride in a solid formulation does not result in

hypoglycemia in a diabetic patient and can be used to safely lower blood glucose levels in type-2 diabetes

4) A generic composition comprising metformin and a sulfonylurea does not provide any insight that the claimed combination is synergistic, nor can inherence be established by probabilities or possibilities.

In response, applicant's arguments in view of the claim amendments are found to be persuasive in regards to claims 1, 3-7 (which are directed to a solid pharmaceutical composition).

The rejection is maintained with respect to the method claims (claims 8-9, and 11) for the reasons discussed below in connection with the rejection 102(e).

REJECTIONS

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8, 9, and 11 are rejected under 35 USC 102(e) as being anticipated by Chandran et al. (US Patent 6,890,957 B2).

Chandran et al. teach a **method of treating hyperglycemia** comprising administering to a patient in need of treatment an antihyperglycemic effective amount of the liquid formulation e.g. **Type II diabetes patient**. Claim 8 recites the term *"[a] method for controlling blood glucose levels in a patient with type 2 diabetes."* Chandran et al. also teach that the primary goal in the treatment of diabetes is to maintain blood glucose levels as close to normal as possible (column 1, lines 46-53, and column 3, lines 27-34; column 9, lines 5-10); instant claim 8 is directed to a *method of controlling blood glucose levels in a patient with type 2 diabetes.* Chanran et al. teach that an acid may be added to the formulation to control pH e.g. hydrochloric acid is preferred (column 7, lines 39-44). Chandran et al. teach liquid compositions of metformin in an amount ranging from **about 20 /ml to about 400 mg/ml**; metformin is administered in a **therapeutic effective amount ranging from about 10 mg/kg/day to about 40 mg/kg/day** (column 4, lines 4-18; column 15, lines 1-60). Chanran et al. teach that the **metformin or salt thereof** may be in combination with one or more antihyperglycemic agents; the antihyperglycemic agent may be an oral antihyperglycemic agent e.g. a sulfonyl urea, such as glybyride, glimepride, glipizide, gluclazide, or chlorpropamide or other known sulfonyl ureas or other antihyperglycemic agents which act on the ATP-dependent channel of the B cells (column 8, lines 1-8). Chandran et al. teach that the **metformin or salt are preferably employed in a weight ratio to the sulfonyl urea in the range from about 50:1 to about 300:1** (column 8, lines 14-17). Claim 8 recites the term *"synergistic combination of glimepiride and metformin or a pharmaceutically acceptable salt thereof, wherein the weight ratio of*

glimepiride and metformin or a pharmaceutically acceptable thereof is about 1/500 to about 2/500;" while claim 11 recites the following amounts of glimepiride/metformin: 500 mg/1mg, 500 mg/2mg, 1000 mg/2mg, and 1000 mg/4mg. The weight ratio taught by Chanran et al. therefore overlaps with the claimed weight ratio/amounts recited in claims 8 and 11 Chandran et al. teach metforim hydrochloride (col. 2, lines 10-27); claims 9 and 11 recite the term "metformin hydrochloride."

Thus, claims 8, 9, and 11 are found to be anticipated for the above reasons.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandran et al. (US Patent 6,890,957 B2), in further view of Moeckel et al. (US Patent 5,955,106), and further in view of Ghebre-Sellassie et al.(US Patent 6,499,984).

The discussion of Chanran et al. in connection with the above rejection under 102(e) is incorporated by reference. Chanran et al. teach liquid formulations for use in children and adults who are not able to swallow tablets (col. 2, lines 10-34). Although Chanran et al. do not teach the instant claimed solid pharmaceutical composition, Chanran et al. do teach that metformin and its salts, especially the hydrochloride are bitter and is usually marketed as a coated tablet wherein the coating is designed to mask any unpleasant taste (col. 2, lines 1-27). The term "[a] solid pharmaceutical composition," as recited in claims 1, 3, 4, 5, 6, and 7, reasonably overlaps with the teaching of the cited prior art as Chanran et al. teach coated metformin tablets.

Instant claim 1 recites the term *"a synergistic combination of glimepiride and metformin or a pharmaceutically acceptable salt thereof, wherein the weight ratio of glimepiride and metformin or a pharmaceutically acceptable salt thereof is about 1/500 to about 2/500,"* which overlaps with the weight ratio range taught by Chanran et al. (col. 8, lines 14-17). Instant claim 2 recites the following weight ratios of metformin hydrochloride to glimepiride of "500mg/1mg; 500 mg/2mg; 1000 mg/2mg; and 1000 mg/4 mg, which also overlaps with the teaching of Chanran. Similarly, the weight ratios of of metformin hydrochloride to glimepiride as recited in claims 4 (500mg/1mg), 5 (500mg/2mg), claim 6 (1000 mg/2mg), and claim 7 (1000mg/4mg), overlap with the teaching of Chandran et al. To the extent that the weight ratios of the prior art and the instant claims overlap, the

synergistic effect of the composition is construed to the an inherent feature of the composition. Chandran et al. teach that that metformin or pharmaceutical salts are in association with a **liquid carrier**, which is reasonably construed to meet the limitation of *"at least one excipient"* recited in instant claims 4, 5, 6, and 7. Chandran et al. teach metformin hydrochloride (col. 2, lines 10-27); claims 3, 4, 5, 6, and 7 recite the term "metformin hydrochloride." Chanran et al. teach metformin and its salts, especially the hydrochloride are bitter; metformin is usually marketed as a coated tablet wherein the coating is designed to mask any unpleasant taste (col. 2, lines 1-27). The term "[a] solid pharmaceutical composition," as recited in claims 1, 3, 4, 5, 6, and 7, reasonably overlaps with the teaching of the cited prior art as Chanran et al. teach coated metformin tablets. However, Chanran et al. do not exemplify solid dosage forms.

Moeckel et al. teach improved methods for preparing metformin solid dosage forms, including tablets and capsules, comprising at least about 70% of metformin relative to the weight of the pharmaceutical composition, wherein the dosage form contain the highest possible content of metformin, and wherein the problem of capping associated with the granulation of metformin is solved (col. 1, line 27 to col. 9, line 56; see especially col. 1, line 27 to 5, line 46).

Ghebre-Sellassie et al.(US Patent 6,499,984) teach methods of preparing tablet dosage forms of antidiabetic drugs, including glimepiride and metformin hydrochloride (see especially col. 9, lines 35-37).

Based on the improved method of preparing metformin taught by Moeckel et al., someone of skill in the art would have been motivated to combine the above cited prior art teachings to create the instant claimed inventive concept for use in type 2 diabetic patients who do not have problems swallowing tablets.

Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-

6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

31 October 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER